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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Needleman, et al.

Serial No.: 08/934,367 **Group No.**: 1642

Filed: September 19, 1997 **Examiner**: M. Davis

For: AN IMMUNOLOGICAL PROCESS AND CONSTRUCTS FOR INCREASING HDL CHOLESTEROL CONCENTRATION BY DNA VACCINATION

July 31, 2001

AMENDMENT
VERSIONS WITH MARKINGS
TO SHOW CHANGES MADE

1. (twice amended) A process for producing antibodies to cholesteryl ester transfer protein (CETP) in a mammal wherein the blood of said mammal contains endogenous CETP [that comprises] comprising the steps of:

(a) immunizing said mammal with an inoculum [containing] comprising a vehicle [in which is dissolved or dispersed] containing a recombinant DNA molecule comprising a DNA sequence that contains (i) a sequence encoding a CETP immunogen linked to (ii) a promoter sequence that controls the expression of said CETP immunogen DNA sequence in said mammal, said CETP immunogen comprising an antigenic carrier to which is covalently bonded one or more immunogenic polypeptides comprising a CETP amino acid residue sequence of about 10 to about 30 residues, said amino acid residue sequence corresponding to an immunogenic sequence of said endogenous CETP; and

(b) maintaining said immunized mammal for a time period sufficient for the production of antibodies that bind to CETP, thereby producing antibodies.

2. (amended) The process of claim [1] 3 wherein the blood of said mammal contains endogenous CETP.

3. (twice amended) A process for increasing the concentration of HDL cholesterol in the blood of a mammal whose blood contains cholesteryl ester transfer protein (CETP) that comprises the steps of:

(a) immunizing said mammal with an inoculum [containing] comprising a vehicle [in which is dissolved or dispersed] containing a recombinant DNA molecule comprising a DNA sequence that contains (i) a sequence encoding a CETP immunogen linked to (ii) a promoter sequence that controls the expression of said CETP immunogen DNA sequence in said mammal, said CETP immunogen comprising an antigenic carrier to which is covalently bonded one or more immunogenic polypeptides comprising a CETP amino acid residue sequence of about 10 to about 30 residues; [and]

(b) maintaining said immunized mammal for a time period sufficient for said CETP immunogen to be expressed and for the production of antibodies that bind to CETP and lessen the transfer of cholesteryl esters from HDL, thereby [reducing] increasing the HDL concentration; and

(c) repeating said immunizing step until the HDL cholesterol value in the blood of said mammal is increased by about 10 percent or more relative to the HDL cholesterol value prior to said first immunization step.

4. (amended) The process according to claim [3] 1 wherein said immunizing step is repeated.

5. (amended) The process according to claim 3 wherein said immunizing step is repeated at intervals of about 3 to about 6 months. [until the HDL cholesterol value in the blood of said mammal is increased by about 10 percent or more relative to the HDL cholesterol value prior to said first immunization step.]

6. (amended) The process according to claim 3 wherein said recombinant DNA molecule encodes human CETP as at least one of said one or more immunogenic polypeptides.

7. (amended) The process according to claim 3 wherein said recombinant DNA molecule encodes rabbit CETP as at least one of said one or more immunogenic polypeptides.

8. (amended) The process according to claim 3 wherein said [encoded] CETP immunogen comprises [an] one immunogenic polypeptide fused to an exogenous antigenic carrier polypeptide.

9. The process according to claim 8 wherein said exogenous antigenic carrier polypeptide is selected from the group consisting of thyroglobulin, tetanus toxoid, and diphtheria toxoid.

10. (amended) The process according to claim [9] 8 wherein said recombinant DNA molecule encodes a fusion protein in which said exogenous antigenic carrier is fused to the carboxy-terminus of said one immunogenic polypeptide.

11. (amended) The process according to claim 8 wherein the carboxy-terminus of said [encoded] exogenous antigenic carrier is fused to the amino-terminus of said [encoded] one immunogenic polypeptide.

15. (amended) The process according to claim 3 wherein at least one of said [encoded] one or more immunogenic polypeptides has the amino acid residue sequence of SEQ ID NOs: 29 or 50.

16. The process according to claim 3 wherein said immunization is carried out by injecting said inoculum into muscle or skin of said mammal.

17. (amended) [An] A human inoculum that comprises a recombinant DNA molecule comprising a DNA sequence that contains (i) a sequence encoding a human CETP immunogen linked to (ii) a promoter sequence that controls the expression

of said CETP immunogen DNA sequence in a [mammal] human, said recombinant DNA molecule [being dissolved or dispersed] contained in an effective amount in a pharmaceutically acceptable vehicle, said CETP immunogen comprising an antigenic carrier to which is covalently bonded one or more immunogenic polypeptides comprising a CETP amino acid residue sequence of about 10 to about 30 residues.

18. The inoculum of claim 17 wherein the concentration of said DNA encoding said CETP immunogen is about 0.05 μg/ml to about 20 mg/ml.

19. The inoculum of claim 17 wherein said vehicle is phosphate-buffered saline.

20. The inoculum of claim 17 wherein said vehicle is isotonic sucrose.

21. The inoculum of claim 17 wherein said DNA is complexed with liposomes.

22. (twice amended) The process according to claim 1 wherein said one or more immunogenic polypeptides [is] are each independently of a sequence selected from the group consisting of SEQ ID Nos: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 29, 32, 33, 34, 35, 36, 37 and 50.

23. (twice amended) The process according to claim 3 wherein said one or more immunogenic polypeptides [is] are each independently of a sequence selected from the group consisting of SEQ ID NOs: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 29, 32, 33, 34, 35, 36, 37 and 50.

24. (amended) The process according to claim 6 wherein at least one of said one or more [encoded] human CETP immunogenic polypeptides comprises a sequence selected from the group consisting SEQ ID NOs: 8-13 and 29.

25. (amended) The process according to claim 7 wherein said [encoded] rabbit CETP immunogenic polypeptide comprises a sequence selected from the group consisting SEQ ID NOs: 2-7 and 50.

26. (amended) The process according to claim 3 wherein said recombinant DNA molecule encodes monkey CETP as at least one of said immunogenic polypeptides.

27. (twice amended) The process according to claim 26 wherein said [encoded] monkey CETP immunogenic polypeptide comprises a sequence selected from the group consisting SEQ ID NOs: 32-36 and 37.

28. (twice amended) The inoculum according to claim 17 wherein at least one of said one or more immunogenic polypeptides is of a sequence selected from

the group consisting of SEQ ID NOs: [2, 3,] 4, [5, 6, 7, 8, 9,] 10, [11, 12, 13,] and 29. [, 32, 33, 34, 35, 36, 37 and 50.]

29. (amended) A recombinant DNA molecule comprising a DNA sequence that contains (i) a sequence encoding a cholesteryl ester transfer protein (CETP) immunogen linked to (ii) a promoter sequence that controls the expression of said CETP immunogen DNA sequence in a mammal, said CETP immunogen being comprised of an exogenous antigenic carrier to which is covalently bonded one or more immunogenic polypeptides of a CETP amino acid residue sequence of about 10 to [about] 30 residues.

30. The recombinant DNA according to claim 29 wherein said promoter sequence is a cytomegalovirus immediate-early promoter sequence.

31. (twice amended) The recombinant DNA according to claim [30] 29 wherein at least one of said one or more immunogenic polypeptides is of a sequence selected from the group consisting of SEQ ID NOs: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 29, 32, 33, 34, 35, 36, 37 and 50.